

FIG. 1

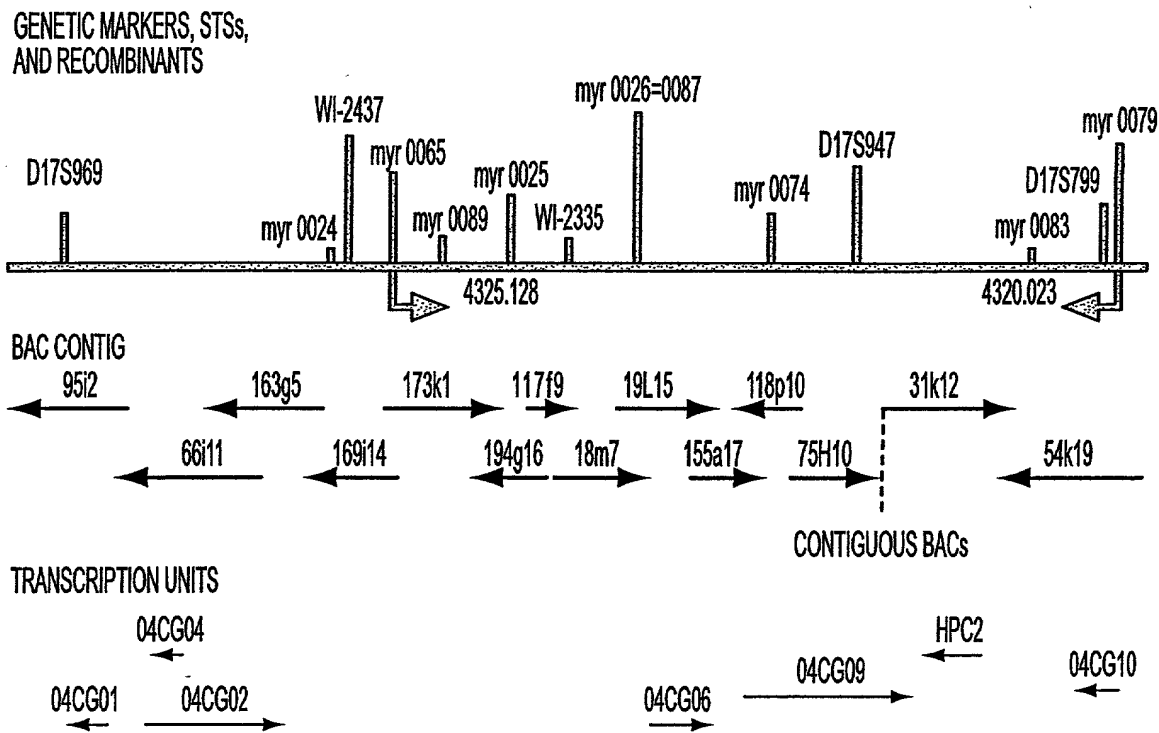


FIG. 2A

BAC 31k12 WITH 2 EXONS OF 04CG09 AND THE HPC2 TRANSCRIPTION UNIT

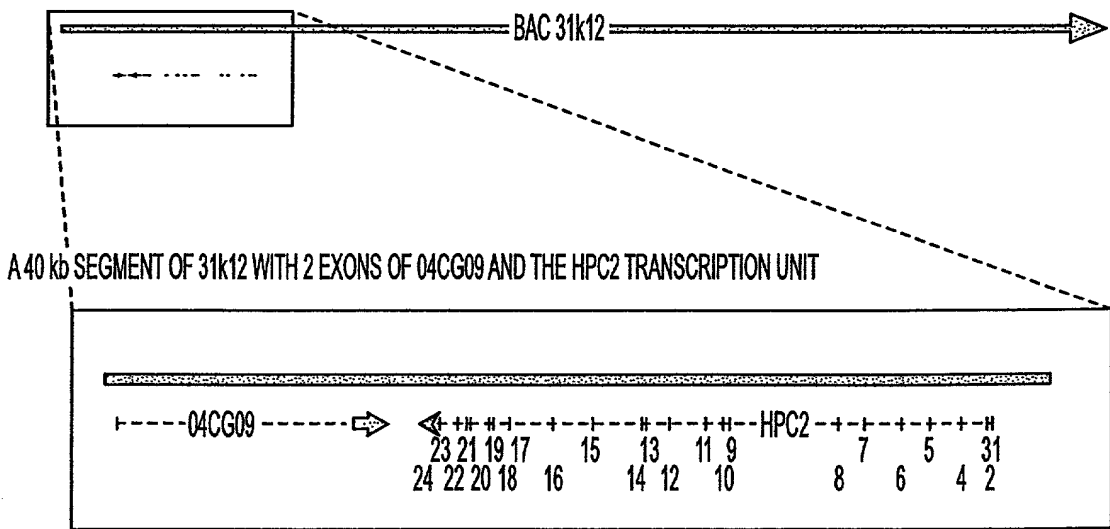


FIG. 2B



Hs.HPC2.exon1	cgcgggcgtaggtgaccggcggttttctcagttttggtggagacggggcg
Hs.HPC2.exon1.pep	
Mm.HPC2.exon2	tggcgggcgtaggggtctgggtgccttgtcagcctggtgtggtcgggtgc
Mm.HPC2.exon1.pep	----- ----- ----- ----- -----
	1 11 21 31 41
Hs.HPC2.exon1	ATGTGGGCGCTTTGCTCGCTGCTGCGGTCCGCGGCCGGACGCACCATGTC
Hs.HPC2.exon1.pep	M--W--A--L--C--S--L--L--R--S--A--A--G--R--T--M--S--
Mm.HPC2.exon2	ATGTGGGCGCTCCGCTCACTGTTGCGTCCCCTTGGCCTGCGCACCATGTC
Mm.HPC2.exon1.pep	M--W--A--L--R--S--L--L--R--P--L--G--L--R--T--M--S--
	----- ----- ----- ----- -----
	51 61 71 81 91
Hs.HPC2.exon1	GCAGGGACGCACCATATCGCAGGCACCCGCCCGCGAGCGGCCGCGCA
Hs.HPC2.exon1.pep	-Q--G--R--T--I--S--Q--A--P--A--R--R--E--R--P--R--K
Mm.HPC2.exon2	GCAGGGT-----TCGGCTCGTCGGCCGCGGCCACCCA
Mm.HPC2.exon1.pep	-Q--G-----S--A--R--R--P--R--P--P--K
	----- ----- ----- ----- -----
	101 111 121 131 141
Hs.HPC2.exon1	AGGACCCGCTGCGGCACCTGCGCACGCGAGAGAAGCGCGGACCGTCGGGG
Hs.HPC2.exon1.pep	--D--P--L--R--H--L--R--T--R--E--K--R--G--P--S--G--
Mm.HPC2.exon2	AAGACCCACTGCGACACCTGCGTACGCGGAGAGAAGCGCGGCCCGGGT---
Mm.HPC2.exon1.pep	--D--P--L--R--H--L--R--T--R--E--K--R--G--P--G-----
	----- ----- ----- ----- -----
	151 161 171 181 191
Hs.HPC2.exon1	TGCTCCGGCGGCCCAAACACCGTGTACCTGCAGGTGGTGGCAGCGGGTAG
Hs.HPC2.exon1.pep	C--S--G--G--P--N--T--V--Y--L--Q--V--V--A--A--G--S--
Mm.HPC2.exon2	---CCCGGGGGCCCAACACCGTGTACCTGCAGGTGGTGGCGGGCGGGCGG
Mm.HPC2.exon1.pep	---P--G--G--P--N--T--V--Y--L--Q--V--V--A--A--G--G--
	----- ----- ----- ----- -----
	201 211 221 231 241
Hs.HPC2.exon1	CCGGGACTCGGGCGCCGCGCTCTACGTCTTCTCCGAGTTCAACCGgtcag
Hs.HPC2.exon1.pep	-R--D--S--G--A--A--L--Y--V--F--S--E--F--N
Mm.HPC2.exon2	CCGGGACGCGGGGGCTGCTCTCTATGTCTTCTCGGAATACAACAGgtcag
Mm.HPC2.exon1.pep	-R--D--A--G--A--A--L--Y--V--F--S--E--Y--N
	----- ----- ----- ----- -----
	251 261 271 281 291
Hs.HPC2.exon1	tcaacgagccacgccccgtcccgctgggccctcagtgcggcgagcctct
Hs.HPC2.exon1.pep	
Mm.HPC2.exon2	agtgggcccagagccctgggggattggccccagcgccacgtgctcgggag
Mm.HPC2.exon1.pep	----- ----- ----- ----- -----
	301 311 321 331 341

FIG. 4

FIGURE 5A

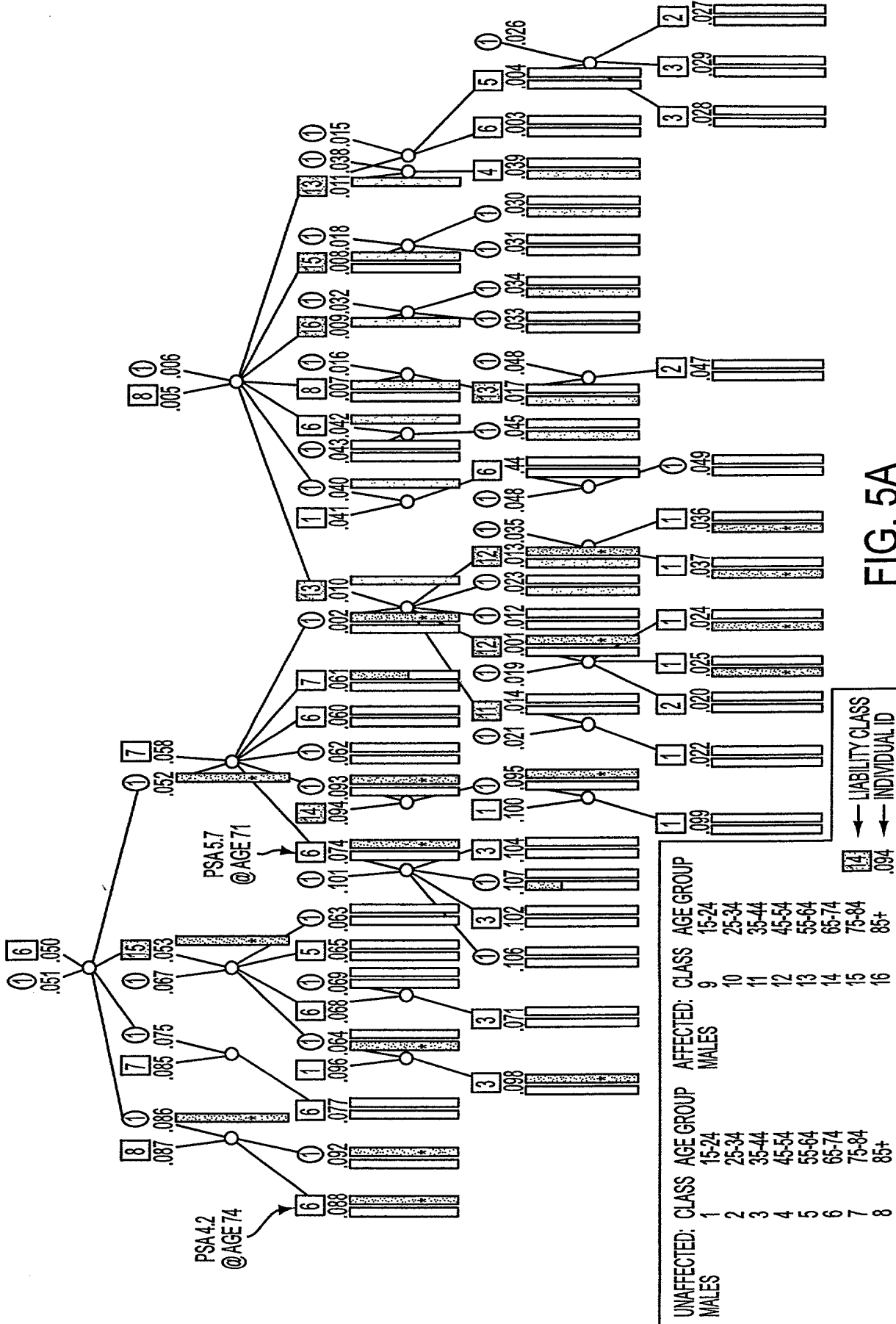


FIG. 5A

FOOTF 28988660

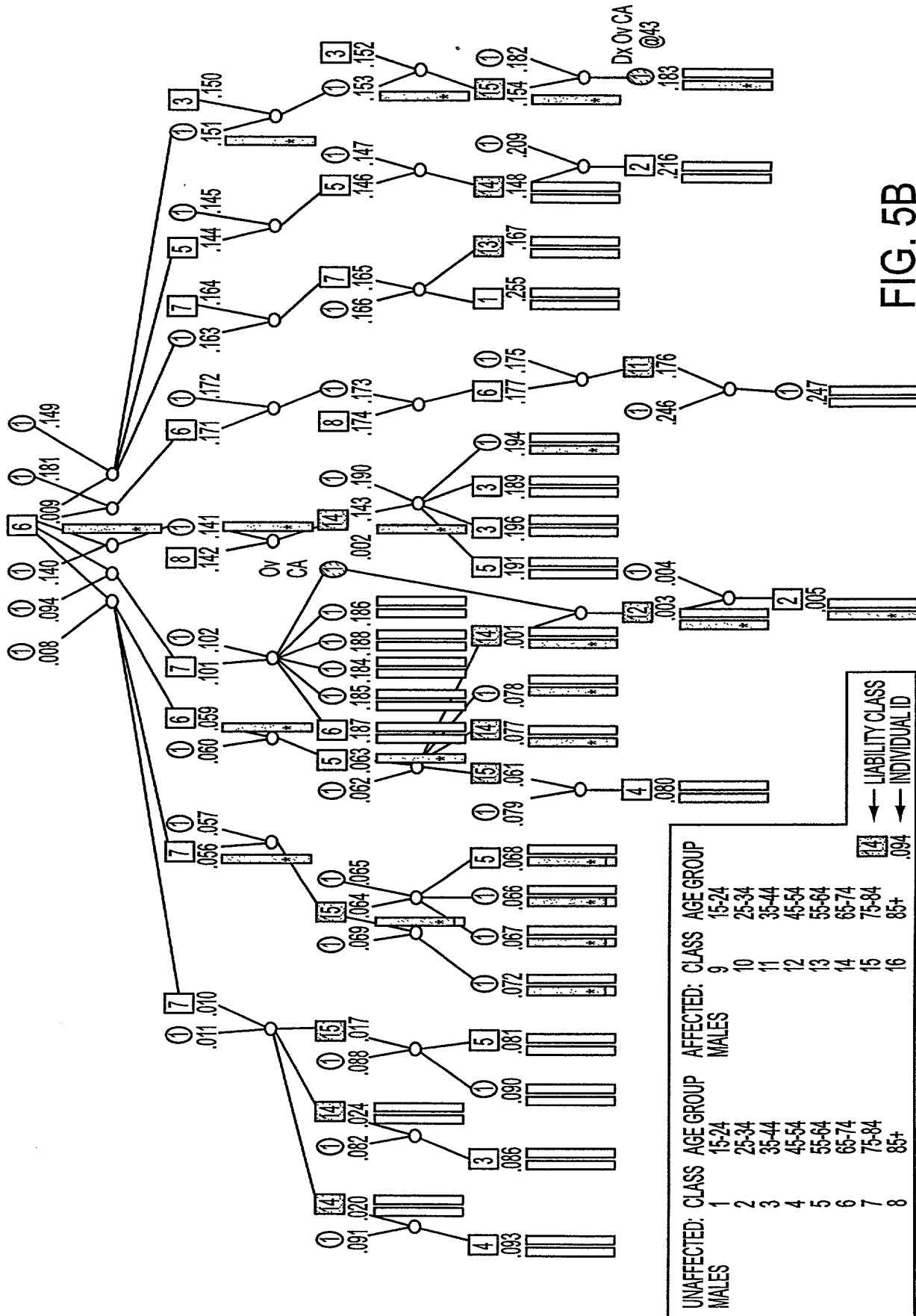


FIG. 5B

TABLE 2838660

(HSA) ELAC2	1	MWALCSLLRSAAAGTWSQGTISQAPARRRPRXKDPLRLHRTREKRGSCGSGGNTVYLQVVA
(MMU) Elac2	1	MWALRSLLRPLGLRTWSQ.....SARRPRPSKDPLRLHRTREKRG.....GPGGNTVYLQVVA
(CEL) CE16965	1	MKNLFFGINKVSRHLISSTCSLFDNNNEELLESIKERTARNRRILQKSSSHLKAREVNASISILRQSMAAVQKKQAHEPPANS·IVNIPSQVSIEVLG
(ATH) gi6850339	1	MENNEATNGSKSSNSGFVNRRRAEGFDITDKKRNLERKSQK·LNPTNTIAYAQILG
(SCE) YKR079C	1	MFTFIPIETH
(HSA) ELAC2	65	AGSRDGAALYWFSEYNR·YLFNCGEVQRLMQEHLKVARLDNIFLT·RMHWSNVGGLSCMLTTLKKEGLPK·CVLSGPPQLEKYL·EAIKIF.....
(MMU) Elac2	57	AGRDAGAALYWFSEYNR·YLFNCGEVQRLMQEHLKVARLDNIFLT·RMHWSNVGGLSCMLTTLKKEGLPK·CVLSGPPQLEKYL·EAIKIF.....
(CEL) CE16965	100	N·GTGLLRACFIILRTPKLT·YMFNCPEACRFLLWQLEIRSSVVDLFIIT·SANWDNITAGISSULLS·KEGNALS·TRLHGANNIKHFL·ECIRPFQDSD
(ATH) gi6850339	58	TGMDTQDTSSVLLFPDKQRFIFENAGEGLQRFCTEHNKIKLSKIDHVFIS·RVCSEFAGGLPCULLTLAGICEEGLSYNVWGPSDLNLYLW·DAMKSFIPRA
(SCE) YKR079C	10	PTSDTKHPLLVSQAHGEKYFFGKIGCGSORSLTENWIRISMLKIDIFLTGELNWSIDGGLPGMILTIAADQKSN·LVLHYGNDILNVIIVSTWRYVYPRF
(HSA) ELAC2	155SGPLK·GIELAVR.....PHSPEYEDETMVYQIPIHSEQRGKHQHQSPERPISRLS·PERSDSESENEPHEL·P.....
(MMU) Elac2	147SGPLK·GIELAVR.....PHSPEYKDETMVYQIPIHSERCGKQPSQSPRTSENRLSPKQSSDSCSAEN·GQCPPE
(CEL) CE16965	193YGSCKY·PSQVEER.....PYTMENYEDAGLKVTYP.....LSP·PLNIGSNNEKS.....
(ATH) gi6850339	156	ANVHTRSGPSPSTPDIPLVNDVVKISALI.....LKP·CHSEEDSCNKSGD.....
(SCE) YKR079C	108GIDLNDHMKDKEVYDKIIIAVKSFNVEKNGGEPRLGVFDSFGKGLRSIVA.....KNFPKHAPTRDYDPSDPHLN.....
(HSA) ELAC2	226	..HGVSQRRGV·RDSLLVVAFLCKHLKRGNELVLKAKEMGRPVGTAAAPILAAVYDKCKSIA·HEGREILAEELCTP.....PDPGAAFWVVECP·DESF
(MMU) Elac2	219	DSSAGANRKAWRDPSLVVAFVCKHLKRGNELVLKAKELGLPVGTAAAPILAAVYDKCKSIA·YEGREILAEELCTP.....PDPGLVFLVVECP·DEGF
(CEL) CE16965	238KNV·KVNVDIAFLIEMKEAARRIDTMKIMELKVE·K·GP·LIGKLSGEAVELPDGRITQDPQVPSDDKVEGDXPLL·LWTECTTETH·
(ATH) gi6850339	203LSVVTVCFLPELCKEDLEKAKK·VFGVKPGPKYSRLQSGESVKS·DERDITVHPSDVMGP·SIPGPIVTLVDCPTTSHA
(SCE) YKR079C	181VELPDLDAKVEVSTNYHISFSPVRGKFKVEEMIKLQVE·K·GP·LFAKLTKGQTHLDNGIWTPEQMLENER·HFAKMLILDIP·DDL
(HSA) ELAC2	317	IQPI·CENATFORVQKADAPVAL·VHM·APASVLVDSRQVQW·MERFEGPDTQ·HLVLMENCASVHNL·RSHKIQTQ·LNIHPDIFELL.....
(MMU) Elac2	313	ILP·ICENDFKRQADTAPVAL·AVH·IAPESVLIDSRQVQW·MERFEGPDTQ·HLILNENCPVHNL·RSHKIQTQ·LSLIHPDIFPOL.....
(CEL) CE16965	322	VKALIDSSSLOPFLNCKQLDY·VWH·ISDDAVINTPTVRL·MEKLNPPSITHLLINGNPNVPAVESVYVHTLIRSIAPSLFEAL.....
(ATH) gi6850339	280	MEHLSKLSLEYSSPDEQIGAKFVNCIHLSPSSVTSPTQSW·MKMFHL·TQ·HILAGQRFPLLIIVSHQAT·VKNMARPILKASSRIAA
(SCE) YKR079C	266	LNAFVEK·FKDYDCA·ELGWVYFLGDEVTINDNLFAFIDIFEKNNGKWNH·MISHNKISNTISFPGSALTITLKALQV·NNYNIPKTRDVFESKDF

FIG. 6A-1

FIG. 6A-2

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(HSA) ELAC2	559	LLQREHALASLGPPLHPLVWAPNQLKAWLQQVHNQCQEVLIHHSWIPAKCLQEGAEISSPAVERLISSLLRTC	
(MMU) Elac2	555	LLQREHALASLGPFPQLLWVAPQLKAWLQQVHNHCQEIHHVSMIPAKCLQGAEVSNITLERLISLLETC	
(CEL) CE16965	565	IARRKEAFESLGADYRPLVWVCNRNWLKPMKTVSICFENIBHLLLEIVDISRYPLTPPGSGGPPGKKRPLRPSPHLPPSRDLQDM	
(ATH) gi6850339	564	LALRSKLLKGVTHPEVIVWGPRLKRFDAVQRLEDLDNEFLDCRSTTATSWASLESAGEAEGSLFTQGSFMQSVFRSDISMNSSLVLC	LK
(SCE) YKR079C	554	LNEWYKYNKDDETSIIYVWTPWQYHAFWNEMLVLENKEILKRIKIVISCHEHINDSFVRMOTQSVPLAEFNEILKENSQESNRKLELDRDSSYRDVD	
(HSA) ELAC1	75	LC-TISLQSGSMVSKQPIENYGPVGLRDFIWRTHLSHTELVFHYVHELVPADQCPABELKEFAHVNRA	PPKEEQRTILLDSEE
(Es c) elac	83	LCSRMSGIIPPLTIYGPQGIREFVETAL	RISGSWTDYPLEIVEIGA
(Syn sp) gi2500943	75	LASSGLAGSGQGIENYGPGLDYLEACC	RFSSHLGKRLKVTHTVRE
(Me t) gi2622965	74	LQSMGFRGEEPLDIYGPPIHELHECTM	KMGYFILDFFDINVEVRG
(HSA) ELAC2	633	DLEEFOTCLVRECKHAFGCALVHT	SGWKWVYSGDTMPCEAL
(MMU) Elac2	629	DLEEFOTCLVRECKHAFGCALVHS	SGWKWVYSGDTMPCEAL
(CEL) CE16965	650	SSSFDKXAKLDELKAVQVHTRMANGVVRV	AGKRIWFSGDTKP
(ATH) gi6850339	657	NLKKVLSHGLNDLISFPVHCPQAYGVVKAER	VNSVGEQLGKWKWVYSGDSRP
(SCE) YKR079C	651	LIRQMYEDLSIEYFOTCRATHCDW	MDENNEHNTFKVSVYSGDTMP
(HSA) ELAC1	163	NSYLLFDDEQFVAKAFRLPERIPSPFESVVEKKRPGKLNQKLDLGVPPGPAYGKLKNCISVVLNGVTISPQDVLKPKPIVGRKICILGDCSG	VVGD
(Es c) elac	130	GEILDDGLRKWTAYPLEHPLECYGRIEEHDYDPCALNAQALKAAGVPPGPIFQELKAKTITLEDGRQINGADYLAAPVPGKALAI	FGDTGCDAA
(Syn sp) gi2500943	122	NGLIYEDKDFQVHCGLLKHRIIPAYGRVVEEKQRPGRFNVEQAEALGIPFGPIYQQLKQKTVTLEDGRRIRRGDLCEPPEPGRKFNVCYCTDTVF	CEEA
(Me t) gi2622965	121	GTVVEDDYRVTAPASGVSFNLANVCFEEKKRPRFLREKAIALGLKPGPAGKLRHRCIPVRVGDRIIMPEVLGSPRKGKWKVYSGDTMP	CESV

FIG. 6B-1

FIG. 6B-2

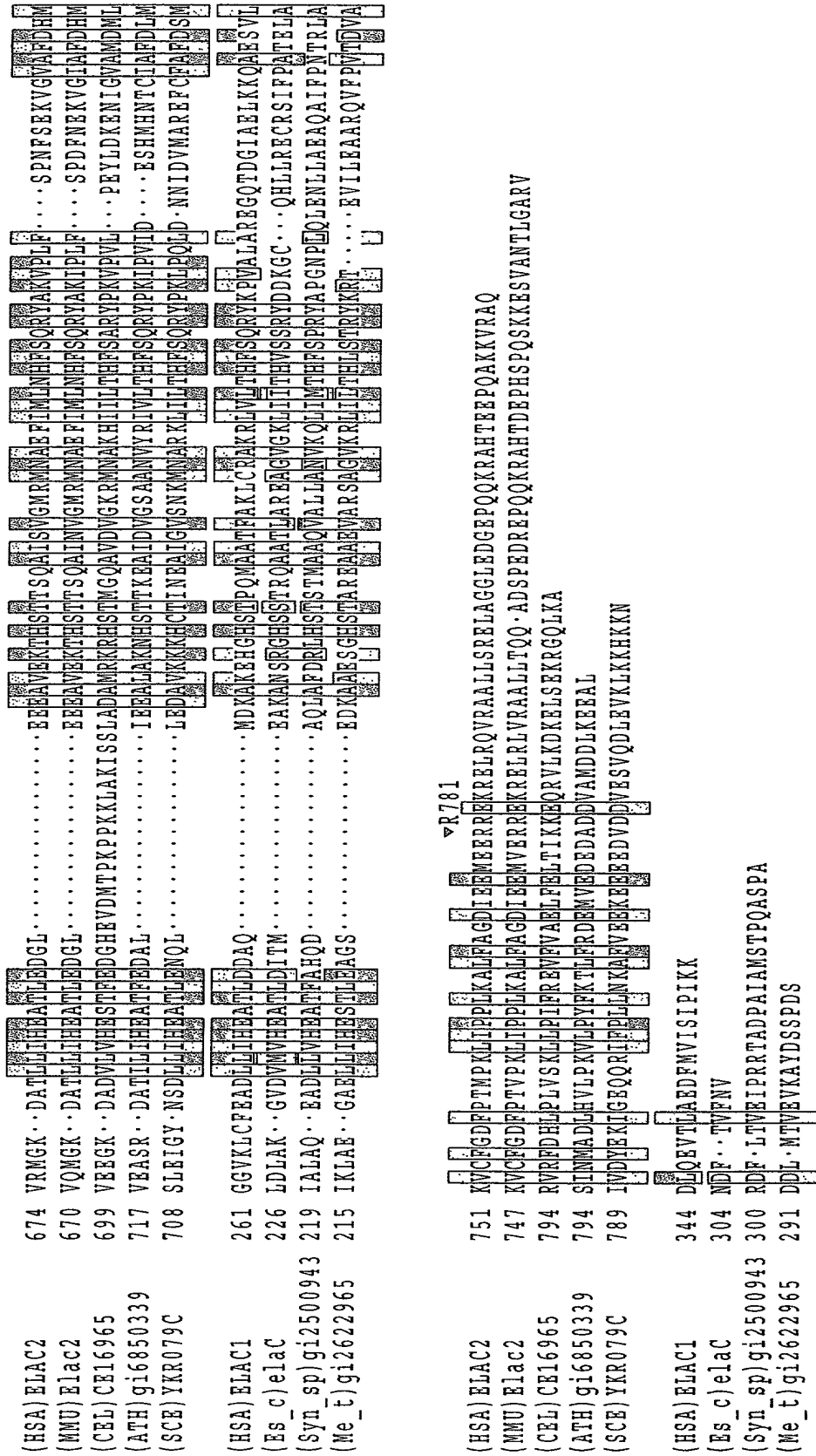


FIG. 6B-2

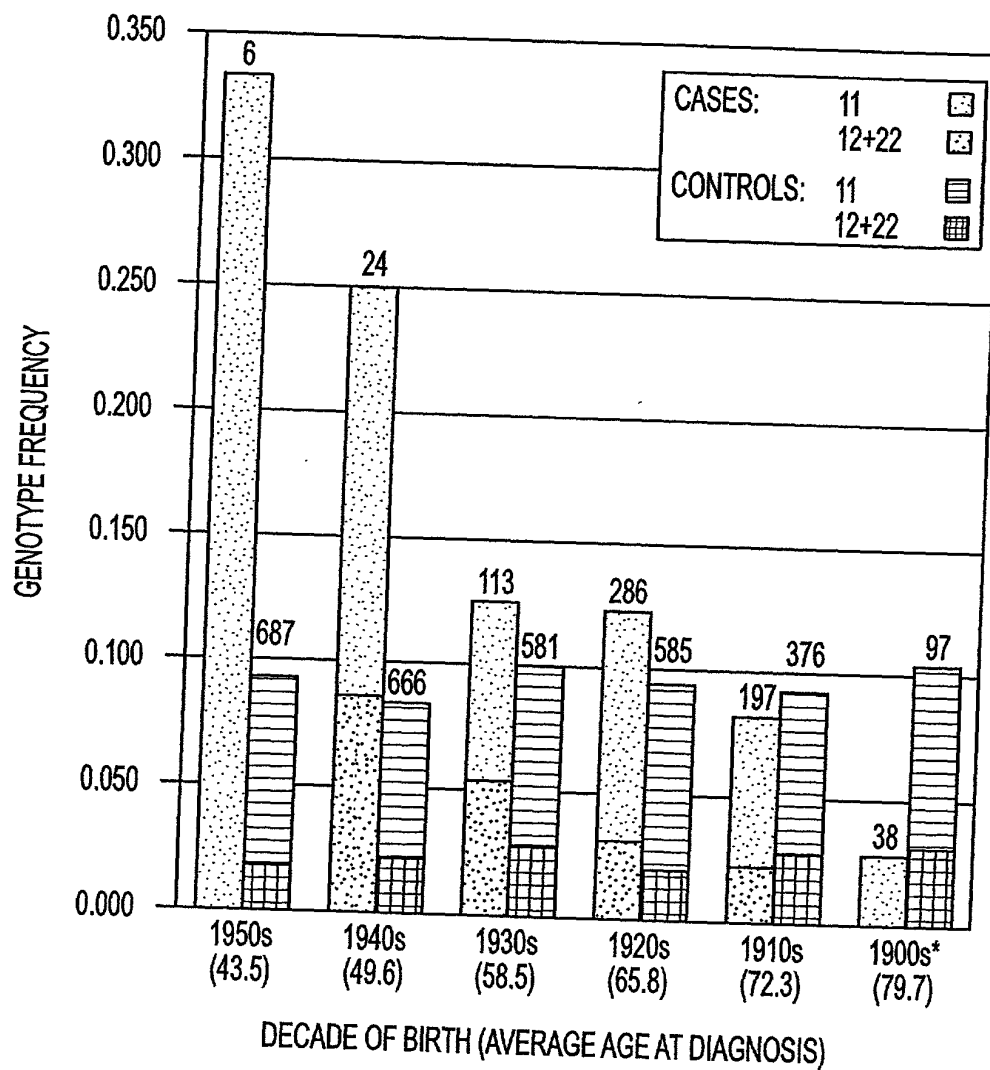


FIG. 7

1920s - 1950s CASES VS. DIVERGENT CONTROLS

		OBSERVED			
		CASES	CONTROLS		
00, 01, 02		372	139	ODDS RATIO P-VALUE	2.4 0.026
11, 12, 22		57 (13.3%)	9 (6.1%)		
00, 01, 11		387	143	ODDS RATIO P-VALUE	3.1 0.022
02, 12, 22		42 (9.8%)	5 (3.4%)		
00, 01		347	137	ODDS RATIO P-VALUE	2.9 0.001
02, 11, 12, 22		82 (19.1%)	11 (7.4%)		

1920s - 1950s CASES VS. PEDIGREE UNAFFECTEDS

00, 01, 02	372	2151	ODDS RATIO P-VALUE	1.5 0.013
11, 12, 22	57 (13.3%)	220 (9.3%)		
00, 01, 02	372	2151	ODDS RATIO 11 ODDS RATIO 12,22 P-VALUE TREND STATISTIC P-VALUE	1.4 2.0 0.017 8.09 0.004
11	40 (9.3%)	170 (7.2%)		
12, 22	17 (4.0%)	50 (2.1%)		

FIG. 8

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CPSF73 family		
(HSA) CPSF73	1	MSAIPAEEDQLLIRPLGAGQEVGRSCILIEFKGRIMLDGCIHPG·LEGNDALPY·IDLIDPAEIDILLISHFELDHCGALPWFLOKT
(ATH) gi6751699	1	MASSTSLKRREQPIISRDGQOLIVTPIGAGSEVGRSCVMSFRGNILDFGCIHPA·YSGMAALPY·FDEIDPSSIDVLLITHFTHDHAASLPVFLKXT
(SCE) YSH1	1	MERTNTTFKFFS LGGSNEVGRSCHILQYKGTWMLDAGIHPA·YQGLASLP·YDEFILSKVDILLISHFELDHGASLPYVMQRT
(Syn_sp) gi2496795	1	MTGSVPDQKAFANISFLPYGVPRD·GGICLEHLGYPYLLDCCLEED·LTPLLAA·DPGTVDLVECSHAHRDHGELGWFHQOF
(Me_t) gi2622312	161	ILQQLGVRIRHQPKYDND·MARLTA·MGGFREVERSCLYIQTPNSRVLLDCGVNVAGDDKNSYPINVPFLLDSLDANILTHAHLDSGFLPYL·YHY
PS02 family		
(HSA) ha3611	651	KRSDHIN·TESPAVNLSTKXVETKSA·HGGLOXGNKKIPSSNVGSRKKTCTPPYKKIKPTGTFTVDAFOYGVVEGCTATLTHFHSHDYAGLSKHFTFP
(ATH) gi2979557	350	TANKLITEFPFGQATEGTIRITAPKPAEKSPDSSSRRAVRNRNGNGSKVIPHMNCIPCTPPFRVDAFKYLTRD·CCHMFLTHFHLDHYQGLTKSFHSG
(SCE) PS02	165	HCDCICGSDPSNMGTPKKNIRSFISNPSSPAKTARDIATSKKPTRVALVLPSPKILKFNNGCHEIVVDGFNYKASETISQFELSHFHSHDYIGLKKSNWP
ELAC2 family		
(HSA) ELAC2	481	PEIIFLGTGSAIPMKIRNVSAIVNISP·DTSLDLCGEGTGGQL·CRHYGQ·VDRVLGTLAAVEVSHLHADHTGSPSILLQR
(ATH) gi6850339	485	MEIVILGTGSSQPSKVRNVSAIFIDIFS·RGSLDLCGEGTGGQL·KRRYGLDGADAEVRKLRCTMISHIHADHTGCLARILALR
(SCE) YXR079C	466	VEIITLGTGSAIPSKVRNVSVLVKVPPTDAGNTI·NRNIMLDAGENTLGTI·HRMFSQLAVKSFODLKMVLSHLEHADHTGLGTSVLNEW
CPSF73 family		
(HSA) CPSF73	148	GKMFHCYHACHVLCANFMFIEA·GVALLYTGDPFS·QEDRHLMAAEIPNIK·PDILIESTYGTTHI·HEAREEREAPFCNTVH
(ATH) gi6751699	158	GKMFHCYHACHVLCANFMVDIA·GVALLYTGDPFS·REEDRHLRAAEIPQS·PDICIEESTSGVQL·HQRHIREKRFTDVIH
(SCE) YSH1	153	GKMFHCYHACHVLCANFMFIEA·GVALLYTGDPFS·REVDRLNSAEVPPPS·SNVLIVESTEGTAT·HEPRLNREKALTQLIH
(Syn_sp) gi2496795	125	GLTVELLPACHLPKANLILLEYNG·DLIRVIVITGDTCLSHLQVLDGLAULTPLRGLK·PDVLLIEGHVGNRR·LPHRRQKEQFIQAI
(Me_t) gi2622312	319	DRLTLHNAACHILGSAWHLHIG·DGQHMVYTGDPK·YEQSRLLEAAANRFR·IETLVWESTYGGHEDVQPSRNRAREKELVKTII
PS02 family		
(HSA) ha3611	783	GKVVLLDANHCPCANMILFYL·NGVILHTGDFRADPSMERSLLADQK·VHMVLDITTYCSPEYTFPSQOEVRFAINTAF
(ATH) gi2979557	484	GIDVTCFDANHCPCGSMILFEPA·NGKAVLHTGDFRYSEENSNWLIGH·ISSJLDTTYCNPDYDFKQEAIVQFVE·AI
(SCE) PS02	308	THSVTLTDANHCPCGAILMLFOEFLA·NSYDKPIRQILHTGDFRSNAKNIETIQKWLAEATANETIDQVLDITTYTNGYNFSPSHSVCTVADFTL

FIG. 9-1

TABLE 2

ELAC2 family	
(HSA) ELAC2	634 ...LEEFQTCLEPHCKHAFGALVHT...SGWNVVSGDMP·CEALVRMGK...DATLLIEATLEDEL
(ATH) gi6850339	667 ...LNDLISFPVHCPOAYGVVKAARVNSVGEQILGWNVYSGDRP·CPETVEASR...DATLLIEATLEDEL
(SCE) YKR079C	660 ...IEYFQTCRAHODWAYNSITFR...MDENNEHTFNVYSGDRPNIKPSLEIGY...NSDLILIEATLEENQL
CPSF73 family	
(HSA) CPSF73	232 ...RGGRLIPVAFALGRAQELLLILDEVQNH...ELH·DIPVY·387 388·VDYISPSAHTDYQOTSEFIRAL...KPPHVLVHGEQNEMARLKAA
(ATH) gi6751699	242 ...QGGRLIPAFALGRAQELLLILDEYWANHP...DLH·NIPVY·397 398·VHYISPSAHADVAQTSTFLKEL...MPPNILLVHGEANEWMLKQK
(SCE) YSH1	237 ...RGGRLIPVAFALGRAQELLLILDEYWSHAD·ELGGQVPVY·399 400·VEELSPAAHVDPOENLEFEKI...SAPNILLVHGEANPMGRUKSA
(Syn_sp) gi2496795	216 ...KGRNILLPVPLGLAQELIKILRTHH...QFTGRQVNLMA·359 360·LEDYLLADHSDGRNTTQLTHNL...RPQHLVEVHGCPSDIEDLTSL
(Me t) gi2622312	407 ...RGGKILLIPVAFANGRAQELMIVLEYYIRTGLIDEVPVIDGMWIR·570 571·KTIEGSGHSDRRQLMEYVYKRIISPKPKILLCHGDNKYKTLDLASS
PS02 family	
(HSA) ha3611	870 ...PHALVCGTYSIGK·EKVFLAIAADVLSKVMSQEKVKTLCQLN·985 986·IYGIPTSEHSSVLEMKRPTQWL...KPKILLPTVNVGTWKSASTME
(ATH) gi2979557	567 ...PKTLFLIGSTIGK·ERLFLERARVLRKLYINPAKLLECLG·685 686·RYEVPYSEHSSSTELKEFTQKV...SPVITIPSVNNDGPDSSAAMV
(SCE) PS02	433 ...YRVFLVGTVTIGK·EKLAIKICEFLKTKLFVMPNSVKFSMLIT·602 603·VFNVPYSEHSSSNDLVKFGCKL...KCSEVITPTVNLNLLWVRYMT
ELAC2 family	
(HSA) ELAC2	633 694·EEEAVKTHSTTSQAI SNGRM...NAEFIMINFSQR·YAKWPLF
(ATH) gi6850339	736 737·IEEALAKNHSTTKEAIDVCSAA...NVYRIVLTHTFSQR·YKPIPV
(SCE) YKR079C	728 729·LEDAYKKKHCTINEAIGSNKM...NARKLITHTFSQR·YKPIPOL

FIG. 9-2

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(HSA) ELAC2			(MMU) Elac2			(CEL) CE16965			(ATH) gi6850339			(SCE) YKR079C		
%ID	%SIM	%GAP	%ID	%SIM	%GAP	%ID	%SIM	%GAP	%ID	%SIM	%GAP	%ID	%SIM	%GAP
100.0	100.0	0.0	-	-	-	-	-	-	-	-	-	-	-	-
81.6	88.0	1.8	100.0	100.0	0.0	-	-	-	-	-	-	-	-	-
24.2	43.0	14.0	24.6	44.0	15.7	100.0	100.0	0.0	-	-	-	-	-	-
25.6	47.0	23.5	25.4	46.0	25.0	21.0	44.0	21.1	100.0	100.0	0.0	-	-	-
21.8	41.0	20.8	21.7	43.0	21.4	18.2	43.0	21.4	21.8	41.0	16.3	100.0	100.0	0.0

(HSA) ELAC2
(MMU) Elac2
(CEL) CE16965
(ATH) gi6850339
(SCE) YKR079C

FIG. 10

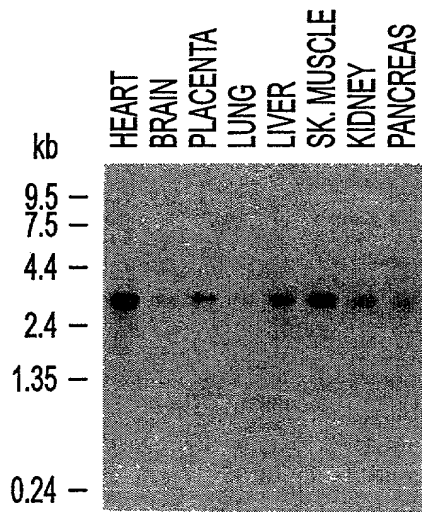


FIG. 11A

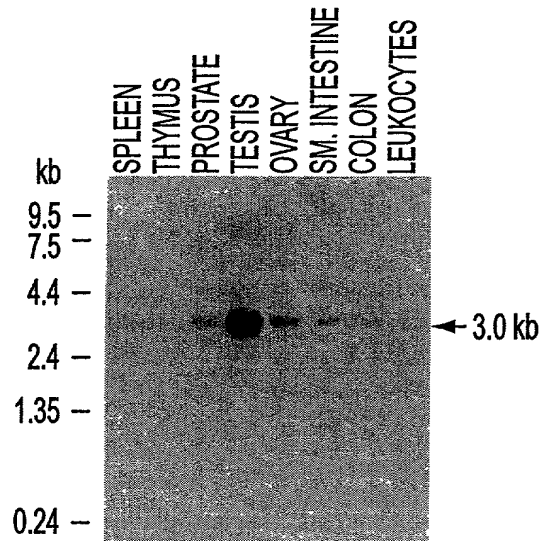


FIG. 11B



FIG. 11C



FIG. 11D

FIG. 12

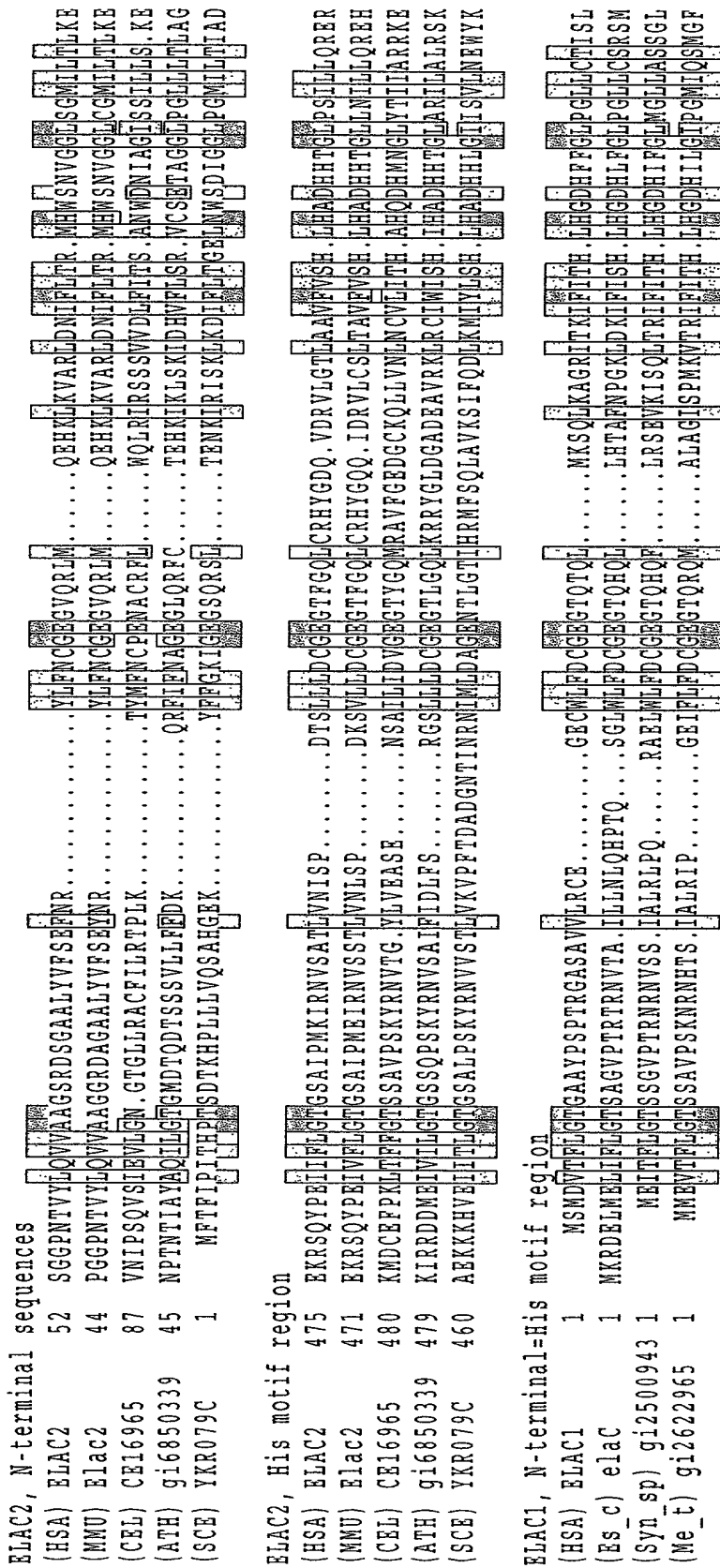


FIG. 12

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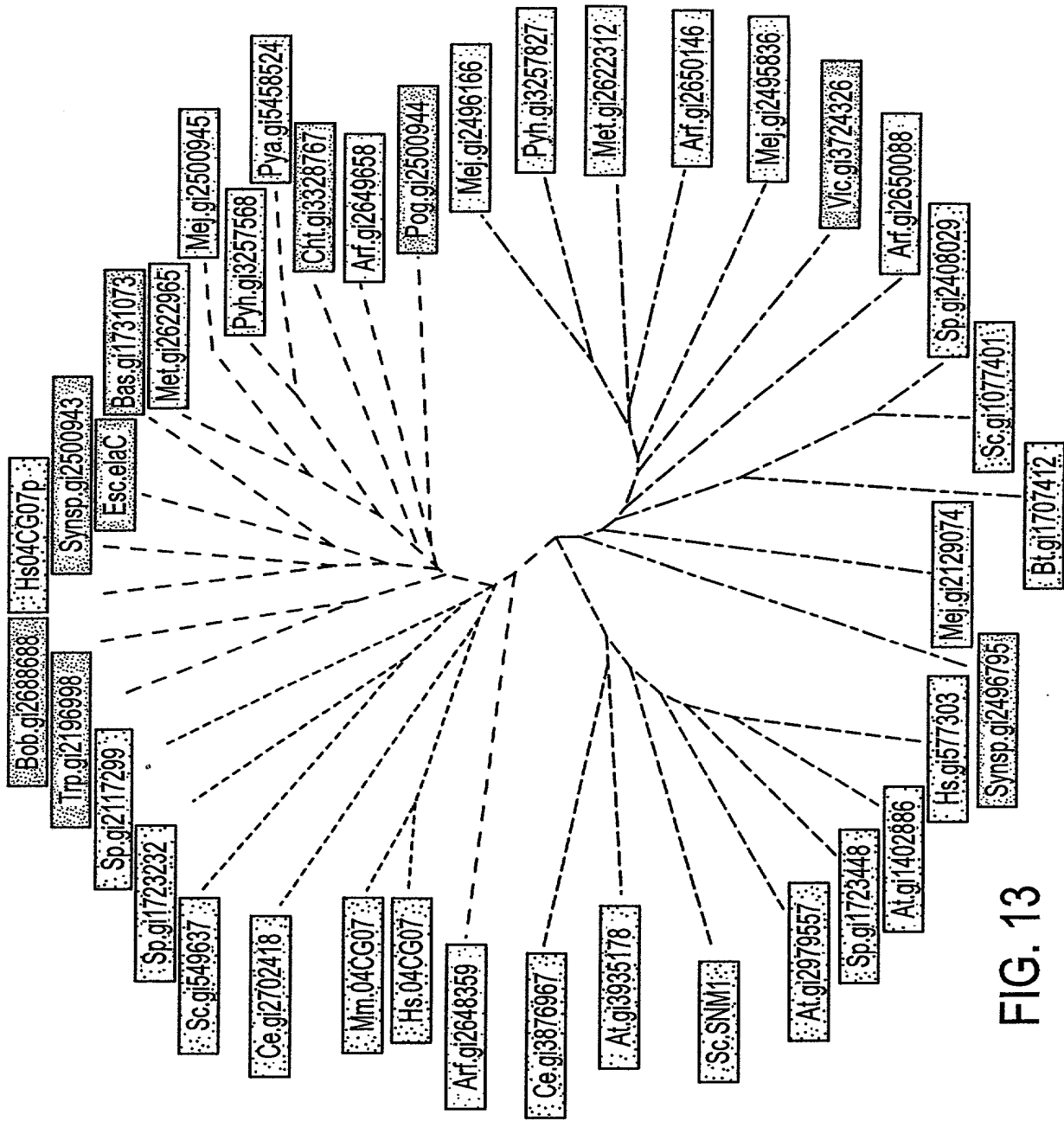
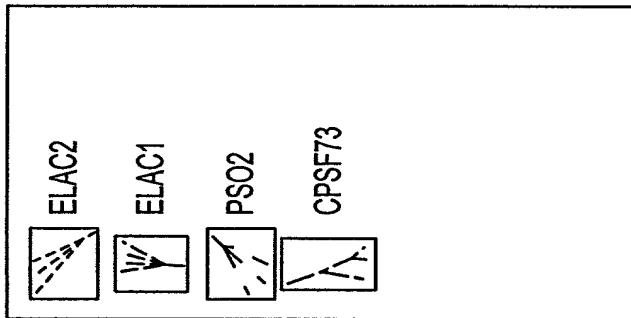


FIG. 13



Eukaryota
 Eubacteria
 Archaea